REMARKS

Status of the Claims

Pending claims

Claims 1 to 92 are pending.

Claims added and amended in the instant amendment

Claims 42 to 55 are amended, claim 1 to 41 and 56 to 92 are canceled, without prejudice, and claims 93 to 110 are added. Thus, after entry of the instant amendment, claims 42 to 55 and 93 to 110 will be pending.

Outstanding Rejections

Claims 42 to 55 stand rejected under 35 U.S.C. §112, first and second paragraphs. Claims 42 to 55 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bronnenmeier, et al. (April, 1995) Applied Environmental Microbiol. 61:1399-1407, and Short, et al., U.S. Patent No. 5,939,250, issued August 17, 1999. Claims 42, 43, 54 and 55 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bronnenmeier, et al. in view of Short, et al., U.S. Patent No. 6,479,258.

Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to nucleic acids having a sequence with at least about 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, or at least 50% homology to an exemplary nucleic acid of the invention and fragments comprising at least about 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto, can be found, inter alia, on page 42, lines 1 to 20. Support for claims directed to polypeptide fragments comprising at least about 10, 15, 20, 25, 30, 35, 40, 50, 75, 100 or 150 residues can be found, e.g., on page 42, lines 20 to 30, and page 46 line 28, to page 47, line 5. Support for claims directed to methods for producing a biologically active polypeptide and screening the

polypeptide for enhanced activity can be found, inter alia, on line 6, page 20 to line 2, page 21. Accordingly, no new matter is added by the instant amendment.

The restriction requirements and election

In the restriction requirement of March 11, 2003, the Patent Office alleged that the pending claims of the application are directed to ten separate and distinct inventions under 35 U.S.C. §121:

In response to the Restriction Requirement of April 9, 2003, Applicants elected Group IV, claims 42 to 55, drawn to a method of generating a variant.

The title

The Patent Office alleged that the title of the invention was not descriptive. The instant amendment addresses this issue with a new title.

Priority

The Patent Office alleged that the priority document (the specification first filed as USSN 08/518,615, on August 23, 1995) does not support the instant claimed invention.

After entry of the instant amendment, claim 42 is drawn to methods of generating a nucleic acid encoding a carboxymethyl cellulase comprising: (a) providing a nucleic acid comprising (i) a sequence encoding a carboxymethyl cellulase and having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (ii) a sequence encoding a carboxymethyl cellulase and comprising at least 30 consecutive nucleotides of a sequence having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (iii) a sequence encoding a carboxymethyl cellulase that hybridizes to a nucleic acid having a sequence as set forth in SEQ ID NO:1 under conditions comprising 42°C in 50% formamide, 5X SSPE, 0.3% SDS, and 200 n/ml sheared and denatured salmon sperm DNA, or, (iv) sequences complementary to (i), (ii) or (iii); (b) varying the sequence of (a) by modifying one or more nucleotides in the sequence to another nucleotide, deleting one or more nucleotides in the sequence, or adding one or more nucleotides to the sequence; and (c) selecting a modified sequence that encodes a carboxymethyl cellulase, thereby generating a nucleic acid encoding a carboxymethyl cellulase.

New claim 110 is drawn to methods of making a variant of a nucleic acid encoding a carboxymethyl cellulase comprising: (a) providing a nucleic acid comprising (i) a

sequence encoding a carboxymethyl cellulase and having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (ii) a sequence encoding a carboxymethyl cellulase and comprising at least 30 consecutive nucleotides of a sequence having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (iii) a sequence encoding a carboxymethyl cellulase that hybridizes to a nucleic acid having a sequence as set forth in SEQ ID NO:1 under conditions comprising 42°C in 50% formamide, 5X SSPE, 0.3% SDS, and 200 n/ml sheared and denatured salmon sperm DNA, or, (iv) sequences complementary to (i), (ii) or (iii); and (b) making a variant sequence of (a) by modifying one or more nucleotides in the sequence to another nucleotide, deleting one or more nucleotides in the sequence, or adding one or more nucleotides to the sequence of (a).

Applicants respectfully aver that the priority document (the specification first filed as USSN 08/518,615) sufficiently supports the claimed invention to satisfy the requirements of section 112, and thus, the pending claims can properly claim priority to USSN 08/518,615. The specification of the priority document clearly describes making and using variants of the polypeptides of the invention, e.g., the carboxymethyl celluloses of the invention, where nucleotide variants include deletion variants, substitution variants and addition or insertion variants. For example, the disclosure states (see column 6, lines 14 to 39, of USPN 6,245,547):

> The present invention further relates to variants of the hereinabove described polynucleotides which encode for fragments, analogs and derivatives of the enzyme having the deduced amino acid sequence of FIG. 1 (SEQ ID NO:2) or the enzyme encoded by the cDNA of the deposited clone. The variant of the polynucleotide may be a naturally occurring allelic variant of the polynucleotide or a non-naturally occurring variant of the polynucleotide. [emphasis added]
>
> Thus, the present invention includes polynucleotides encoding the same mature enzyme as shown in FIG. 1 (SEQ ID NO:2) or the same mature enzyme encoded by the cDNA of the deposited clone as well as variants of such polynucleotides which variants encode for a fragment, derivative or analog of the enzyme of FIG. 1 (SEQ ID NO:2) or the enzyme encoded by the cDNA of the deposited clone. Such nucleotide variants include deletion variants, substitution variants and addition or insertion variants. [emphasis added]
>
> As hereinabove indicated, the polynucleotide may have a coding sequence which is a naturally occurring allelic variant of the coding sequence shown in FIG. 1 (SEQ ID NO:1) or of the coding sequence of the deposited clone. As known in the art, an allelic variant is an alternate form of a polynucleotide sequence which may have a substitution,

> deletion or addition of one or more nucleotides, which does not substantially alter the function of the encoded enzyme. [emphasis added]

The specification of the priority document also clearly describes identifying variants of the polypeptides of the invention, e.g., the carboxymethyl celluloses of the invention. For example, the disclosure states (see column 6, lines 14 to 39, of USPN 6,245,547):

> Another aspect of the invention is an assay for identifying fragments or variants of SEQ ID NO:2, and sequences substantially identical thereto, which retain the enzymatic function of SEQ ID NO:2, and sequences substantially identical thereto. The assay includes contacting SEQ ID NO:2, sequences substantially identical thereto, or polypeptide fragment or variant with a substrate molecule under conditions which allow the polypeptide fragment or variant to function, and detecting either a decrease in the level of substrate or an increase in the level of the specific reaction product of the reaction between the polypeptide and substrate thereby identifying a fragment or variant of such sequences. [emphasis added]

Accordingly, because the claimed invention, including the pending claims after entry of the instant amendment, is sufficiently supported by the specification of the priority document to satisfy the requirements of section 112, priority to the specification first filed as USSN 08/518,615, can be properly made.

Sequence compliance

The instant amendment places the specification in compliance with the sequence rules. The attached sheet of drawings includes changes to Figure 5C, which place the figure in compliance with the sequence rules.

Issues under 35 U.S.C. §112, second paragraph

Claims 42 to 55 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

> *The phrases "sequences complementary thereto" and "substantially identical" and "fragments comprising ... thereof"*

The Patent Office alleged claims 42 to 55 are indefinite because of the phrases "sequences complementary thereto", "fragments comprising ... thereof" and "substantially identical." The instant amendment addresses this issue. The phrases have been deleted.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 42 to 55 under 35 U.S.C. §112, first paragraph, have been rejected for allegedly containing subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Patent Office alleged, inter alia, that the instant claims are drawn to methods for generating a variant comprising obtaining a genus of nucleic acids having any function. The instant amendment addresses this issue. After entry of this amendment, claim 42 will be drawn to a method of generating a nucleic acid encoding a carboxymethyl cellulase comprising providing a nucleic acid comprising (i) a sequence encoding a carboxymethyl cellulase and having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (ii) a sequence encoding a carboxymethyl cellulase and comprising at least 30 consecutive nucleotides of a sequence having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (iii) a sequence encoding a carboxymethyl cellulase that hybridizes to a nucleic acid having a sequence as set forth in SEQ ID NO:1 under conditions comprising 42°C in 50% formamide, 5X SSPE, 0.3% SDS, and 200 n/ml sheared and denatured salmon sperm DNA, or, (iv) sequences complementary to (i), (ii) or (iii).

It is alleged that the specification must disclose the critical structural elements of a polypeptide required to have carboxymethyl cellulase activity for Applicants to reasonably describe they had possession of the claimed invention. It is also alleged that the specification must disclose which fragments of a nucleic acid encode a carboxymethyl cellulase for Applicants to reasonably describe they had possession of the claimed invention. The Patent Office alleged that because the specification discloses only a single species of a genus of nucleic acids required to practice the claimed invention, one skilled in the art could not have reasonably concluded that Applicants had possession of the claimed invention at the time the application was filed.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the

claimed invention at the time of filing. Applicants respectfully submit that describing a genus of polynucleotides in terms of its physico-chemical properties (e.g., a % sequence identity) as compared to an exemplary species (e.g., SEQ ID NO:1, encoding SEQ ID NO:2) and function (e.g., encoding a polypeptides having carboxymethyl cellulase) satisfies the written description requirement of section 112, first paragraph.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph, and note that the guidelines state that a description of a genus of polynucleotides in terms of its physico-chemical properties, e.g., a % sequence identity, to a single exemplary species, and a common function satisfies the written description requirement of section 112, first paragraph, for the genus of polynucleotides.

In Example 14 of the Guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of Example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of nucleic acids of the invention is described by structure (the exemplary nucleic acid SEQ ID NO:1, or encoding SEQ ID NO:2), a physico-chemical property (percent sequence identify) and function (having carboxymethyl cellulase). All nucleic acids of the genus used in the claimed methods must have at least 50% or more sequence identity to a sequence as set forth SEQ ID NO:1 or SEQ ID NO:2. The USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical

property (e.g., a % sequence identity) and a defined function, the genus of claimed polypeptides also meet the written description requirements of section 112.

The genus of nucleic acids of the invention also fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the claimed carboxymethyl cellulase-encoding nucleic acids. The claimed genus of polypeptides all must have carboxymethyl cellulase activity and a specific physical characteristic, e.g., a % sequence identity to the exemplary nucleic acid. Therefore, the genus of nucleic acids used in the claimed methods is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

> Similarly, in this court's most recent pronouncement, it noted:
>
> > More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.
>
> Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of carboxymethyl cellulases encoded by the nucleic acids of the invention is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity).

Accordingly, the sequences of the invention are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Applicants also respectfully refer to recently issued claims directed to genuses of polynucleotides based on sequence identity (and stringent hybridization) to an exemplary nucleic acid, see, e.g., recently issued claims directed to, e.g., 72.5% sequence identity, as in USPN 6,593,514; 75% sequence identity, as in USPN 6,586,215; 80% sequence identity, as in USPN 6,596,926; 85% sequence identity, as in USPN 6,590,141 and USPN 6,586,179; 86% sequence identity, as in USPN 6,583,337; 90% sequence identity (and "stringent hybridization"), as in USPN 6,541,684 (see Exhibit B).

The Patent Office alleged, inter alia, that a single species is insufficient to put one of skill in the art in possession of the attributes and features of all species with the claimed genus. As discussed above, Applicants respectfully aver that there is no bright line rule that a single species is insufficient to put one of skill in the art in possession of the attributes and features of all species with a genus. In fact, both the Patent Office and the Federal Circuit set forth conditions where a single species is sufficient to put one of skill in the art in possession of the attributes and features of all species within a genus, where the genus is defined in terms of shared physical and structural properties with the single species.

Enablement

Claims 42 to 55 are rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not reasonably provide enablement for the claimed invention.

The Patent Office does state that the specification is enabling for a method for generating variants comprising obtaining a nucleic acid comprising the polynucleotide of SEQ ID NO:1 and modifying this nucleic acid.

However, it is alleged that the specification does not provide reasonable enablement for a method of generating variants comprising obtaining any nucleic acid which has at least 50% sequence identity to any fragment of the polypeptide of SEQ ID NO:1, and to modify that nucleic acid. Regarding any concerns that the claimed methods for generating a variant may comprise obtaining a genus of nucleic acids having any function, the instant

amendment addresses this issue. After entry of this amendment, claim 42 will be drawn to a method of generating a nucleic acid encoding a carboxymethyl cellulase comprising providing a nucleic acid comprising (i) a sequence encoding a carboxymethyl cellulase and having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (ii) a sequence encoding a carboxymethyl cellulase and comprising at least 30 consecutive nucleotides of a sequence having at least 50% sequence identity to a nucleic acid as set forth in SEQ ID NO:1, (iii) a sequence encoding a carboxymethyl cellulase that hybridizes to a nucleic acid having a sequence as set forth in SEQ ID NO:1 under conditions comprising 42°C in 50% formamide, 5X SSPE, 0.3% SDS, and 200 n/ml sheared and denatured salmon sperm DNA, or, (iv) sequences complementary to (i), (ii) or (iii).

It is also alleged that the specification does not provide reasonable enablement because it does not disclose the critical structural elements required in any nucleic acid to encode a polypeptide which has carboxymethyl cellulase activity and it does not describe which fragments of such nucleic acid would encode a polypeptide having carboxymethyl cellulase activity. It is also alleged that because the specification does not provide reasonable enablement it would take undue experimentation to practice the invention.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of nucleic acids encoding carboxymethyl cellulases to practice the claimed invention. As declared by Dr. Jay Short (see attached Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for carboxymethyl cellulase activity, was very high. As declared by Dr. Short, using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of nucleic acids encoding the exemplary carboxymethyl cellulase of the invention and screen them for expression of polypeptides having carboxymethyl cellulase activity. Dr. Short declares that one skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to screen for nucleic acids encoding polypeptides having at least 50% percent sequence identity to SEQ ID NO:1, or active fragments thereof, for carboxymethyl cellulase activity. As declared by Dr. Short, while the numbers of samples

needed to be screened may have been high, the screening procedures were routine and successful results (i.e., finding variant nucleic acids encoding carboxymethyl cellulases) predictable. Furthermore, Dr. Short declares that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with carboxymethyl cellulase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides having carboxymethyl cellulase activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including identification of a genus of nucleic acids encoding carboxymethyl cellulases.

Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen numbers of negatives to find a sample that has the desired properties, e.g., carboxymethyl cellulase activity. Furthermore, as declared by Dr. Short, the screening procedures used to identify nucleic acids within the scope of the instant invention (e.g., identifying nucleic acids encoding carboxymethyl cellulases) were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could practice the instant claimed invention without undue experimentation.

Enablement is not precluded by the necessity to screen large numbers of alternative compounds (e.g., nucleic acids or polypeptides), as long as that screening is "routine," i.e., not "undue." As declared by Dr. Short, it would have taken only routine protocols to making variants of the exemplary nucleic acids and screen them to identify those that encode polypeptides with carboxymethyl cellulase activity. Thus, the specification enabled the skilled artisan at the time of the invention to make and use a broad genus of carboxymethyl cellulases used in the methods of the present invention.

Accordingly, Applicants respectfully submit that the pending claims meet the written description and enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §103(a)

Bronnenmeier, et al. and U.S. Patent No. 5,939,250

Claims 42 to 55 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bronnenmeier, et al., (April, 1995) Applied Environmental Microbiol. 61:1399-1407, and Short, et al., U.S. Patent No. 5,939,250, issued August 17, 1999, having a priority document filed on December 7, 1995 (herein after "the '250 patent").

The Patent Office notes that Bronnenmeier, et al. teaches the purification of cellulase enzymes from *T. maritima*. The Patent Office also states that Bronnenmeier, et al. does not teach the polynucleotide sequence encoding these enzymes.

Applicants respectfully agree with the Patent Office that Bronnenmeier, et al. does not teach the polynucleotide sequence of the enzymes isolated by the methods described by Bronnenmeier, et al. In fact, Bronnenmeier, et al., does not teach the structure or sequence of any enzyme, including any carboxymethyl cellulase, including the enzymes of the instant invention.

The Patent Office alleges that because the source of enzymes isolated by Bronnenmeier, et al. and the instant invention are the same, the enzymes are "one and the same."

Applicants respectfully aver that Bronnenmeier, et al., does not teach the structure or sequence of any enzyme, including any carboxymethyl cellulase, including the enzymes of the instant invention. The Patent Office has presented no evidence that the enzymes isolated by Bronnenmeier, et al., have any similarity in structure to the enzymes of the claimed invention. Because Bronnenmeier, et al., does not teach the structure of any enzyme, it does not teach how to make the enzymes of the instant invention. Accordingly, Bronnenmeier, et al., is a defective reference in that it does not teach the structure of the enzymes of the claimed invention, or how to make and use them.

The Patent Office cited the '250 patent for teaching a number of mutagenesis techniques.

As discussed above, because the claimed invention, including the pending claims after entry of the instant amendment, is sufficiently supported by the specification of the priority document to satisfy the requirements of section 112, priority to the specification first filed as USSN 08/518,615, on August 23, 1995, can be properly made. The '250 patent has as its earliest priority document a provisional patent application filed on December 7, 1995. Accordingly, the '250 patent is not prior art to the instant invention and cannot be used to cure the defects in Bronnenmeier, et al.

Furthermore, the '250 patent does not teach the structure of any enzymes, including the enzymes of the claimed invention. Thus, even if the '250 patent were prior art to the instant invention, it would not cure the defects in Bronnenmeier, et al.

Applicants respectfully submit that the basis for the Patent Office's argument is improper. It was alleged that because the source of enzymes isolated by Bronnenmeier, et al. and the instant invention are the same, the enzymes are "one and the same." Bronnenmeier, et

al. teaches no structures. The courts have explicitly rejected this basis for rejecting compositions. See In re Bell, 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993), and In re Deuel, 51 F.3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995). In both Bell and Deuel, the Patent Office alleged that composition claims directed to nucleic acid sequences were obvious in view of references that taught general methods for making oligonucleotides and then using them to isolate desired nucleic acid sequences. In Deuel, the Federal Circuit reversed the PTO, reasoning that:

> The PTO's focus on known methods for potentially isolating the claimed DNA molecules is also misplaced because the claims at issue define compounds, not methods .... We today reaffirm the principle, stated in Bell, that the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the claimed DNAs. In re Deuel, 51 F.3d at 1555.

Analogously, the existence of a general method of isolating an enzyme is essentially irrelevant to the question whether the specific molecules themselves would have been obvious, in the absence of other prior art that suggests the structure of the claimed molecules.

Obviousness for chemical compounds is based on a showing of structural similarity. See In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990) (en banc).

Accordingly, because Bronnenmeier, et al. in view of the '250 patent do not teach or suggest the claimed invention, the Patent Office did not present a *prima facie* case of obviousness, and the rejection under section 103 can be properly withdrawn.

Bronnenmeier, et al. and U.S. Patent No. 6,479,258

Claims 42, 43, 54 and 55 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Bronnenmeier, et al. in view of Short, et al., U.S. Patent No. 6,479,258, issued November 12, 2002, having a priority document filed on December 7, 1995 (herein after "the '258 patent").

The Patent Office notes that Bronnenmeier, et al., does not use the methods of mutagenesis specifically recited in claims 44 to 53 to produce mutant carboxymethyl cellulases.

However, as discussed above, Bronnenmeier, et al., is further defective in that it does not teach or suggest the structure of any enzyme of the invention.

The Patent Office cited the '258 patent for teaching a number of known techniques for non-stochastic methods of directed mutagenesis.

As discussed above, because the claimed invention, including the pending claims after entry of the instant amendment, is sufficiently supported by the specification of the priority document to satisfy the requirements of section 112, priority to the specification first filed as USSN 08/518,615, on August 23, 1995, can be properly made. The '258 patent has as its earliest priority document a provisional patent application filed on December 7, 1995. Accordingly, the '258 patent is not prior art to the instant invention and cannot be used to cure the defects in Bronnenmeier, et al.

Furthermore, the '258 patent does not teach the structure of any enzymes, including the enzymes of the claimed invention. Thus, even if the '258 patent were prior art to the instant invention, it would not cure the defects in Bronnenmeier, et al.

Accordingly, because Bronnenmeier, et al. in view of the '258 patent do not teach or suggest the claimed invention, the Patent Office did not present a *prima facie* case of obviousness, and the rejection under section 103 can be properly withdrawn.

Obviousness under 35 U.S.C. 102(e)/103(c)

The instant application was filed on or after November 29, 1999, and the claimed application and the subject matter of the Short, et al., '258 patent were, at the time the instant invention was made, owned by the same entity. Accordingly, under former 35 U.S.C. 103(c) the '258 patent is disqualified as prior art against the claimed invention.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. §103(a). Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby

authorized to charge any such fees to Deposit Account No. 06-1050. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: Sept. 23, 2003

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GAG TTT GGT GCC TAC AGA AAA GCT GAC CTT GAA TCA AGA ATA AAA TGG ACC TCC
 E   F   G   A   Y   R   K   A   D   L   E   S   R   I   K   W   T   S

TTT GTC GTT CGC GAA ATG GAG AAA AGG AGA TGG AGC TGG GCA TAC TGG GAA TTT
 F   V   V   R   E   M   E   K   R   R   W   S   W   A   Y   W   E   F

TGT TCC GGT TTT GGT GTT TAT GAT ACT CTG AGA AAA ACC TGG AAT AAA GAT CTT
 C   S   G   F   G   V   Y   D   T   L   R   K   T   W   N   K   D   L

TTA GAA GCT TTA ATA GGA GGA GAT AGC ATT GAA TAA
 L   E   A   L   I   G   G   D   S   I   E   *
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SEQ ID NO. 1
SEQ ID NO. 2

FIGURE 5C

Example 14: Product by Functi n

Specification: The specification exemplifies a protein isolated from liver that catalyzes the reaction of A → B. The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:

A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A → B.

Analysis:

A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.

A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3. Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".

The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.

A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that

applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

EXHIBIT B

United States Patent **6,596,926**
Fam du , et al. **July 22, 2003**

Phosphatidylcholine biosynthetic enzymes

Abstract

This invention relates to an isolated nucleic acid fragment encoding phosphatidylethanolamine N-methyltransferase biosynthetic enzyme. The invention also relates to the construction of a chimeric gene encoding all or a portion of the phosphatidylethanolamine N-methyltransferase biosynthetic enzyme, in sense or antisense orientation, wherein expression of the chimeric gene results in production of altered levels of phosphatidylethanolamine N-methyltransferase biosynthetic enzyme in a transformed host cell.

Inventors: **Famodu; Omolayo O.** (Newark, DE); **Kinney; Anthony J.** (Wilmington, DE); **Rafalski; J. Antoni** (Wilmington, DE)

Assignee: **E. I. du Pont de Nemours and Company** (Wilmington, DE)

Appl. No.: **668262**

Filed: **September 22, 2000**

Current U.S. Class: **800/281**; 435/6; 435/69.1; 435/183; 435/410; 435/419; 435/252.3; 435/320.1; 530/350; 530/370; 536/23.2; 536/23.6; 536/24.1; 536/24.3; 536/24.33; 800/278; 800/295

Intern'l Class: A01H 003/00; C07H 021/04; C07K 014/415; C12N 005/14; C12N 009/00

Field of Search: 435/6,69.1,183,410,419,252.3,320.1 530/350,370 536/23.2,23.6,24.1,24.3,24.33 800/278,295,281

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Primary Examiner: Bui; Phuong T.

Parent Case Text

This application claims the benefit of U.S. Provisional Application No. 60/155,626, filed Sep. 23, 1999.

Claims

What is claimed is:

1. An isolated ***polynucleotide*** comprising:

(a) a nucleotide sequence encoding a polypeptide having phosphatidylethanolamine N-methyltransferase activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:20 have at least 80% sequence ***identity*** based on the Clustal alignment method, or

(b) the complement of the nucleotide sequence, wherein the complement and the nucleotide sequence contain the same number of nucleotides and are 100% complementary.

2. The ***polynucleotide*** of claim 1 wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:20 have at least 85% sequence ***identity*** based on the Clustal alignment method.

3. The ***polynucleotide*** of claim 1 wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:20 have at least 90% sequence ***identity*** based on the Clustal alignment method.

4. The ***polynucleotide*** of claim 1 wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:20 have at least 95% sequence ***identity*** based on the Clustal alignment method.

5. The ***polynucleotide*** of claim 1 wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:20.

6. The ***polynucleotide*** of claim 1 wherein the nucleotide sequence comprises the

nucleotide sequence of SEQ ID NO:19.

7. A vector comprising the ***polynucleotide*** of claim 1.

8. A recombinant DNA construct comprising the ***polynucleotide*** of claim 1 operably linked to a regulatory sequence.

9. A method for transforming a cell comprising transforming a cell with the ***polynucleotide*** of claim 1.

10. A cell comprising the recombinant DNA construct of claim 8.

11. A method for producing a plant comprising transforming a plant cell with the ***polynucleotide*** of claim 1 and regenerating a plant from the transformed plant cell.

12. A plant comprising the recombinant DNA construct of claim 8.

13. A seed comprising the recombinant DNA construct of claim 8.

United States Patent **6,593,514**
Cahoon , et al. **July 15, 2003**

Method for the production of calendic acid, a fatty acid containing delta-8,10,12 conjugated double bonds and related fatty acids having a modification at the delta-9 position

Abstract

The preparation and use of nucleic acid fragments encoding plant fatty acid modifying enzymes associated with modification of the delta-9 position of fatty acids, in particular, formation of conjugated double bonds are disclosed. Chimeric genes incorporating such nucleic acid fragments and suitable regulatory sequences can be used to create transgenic plants having altered lipid profiles. The preparation and use of nucleic acid fragments encoding plant fatty acid modifying enzymes associated with formation of a trans delta-12 double bond also are disclosed. Chimeric genes incorporating such nucleic acid fragments and suitable regulatory sequences can be used to create transgenic plants having altered lipid profiles.

Inventors: **Cahoon; Edgar Benjamin** (Wilmington, DE); **Hitz; William Dean** (Wilmington, DE); **Ripp; Kevin G.** (Wilmington, DE)

Assignee: **E. I. du Pont de Nemours and Company** (Wilmington, DE)

Appl. No.: **638937**

Filed: **August 15, 2000**

Current U.S. Class: **800/281**; 800/298; 435/69.1; 435/419; 536/23.6

Intern'l Class: A01H 005/00; C12N 015/82; C07H 021/04

Field of Search: 800/281,298 435/69.1,419 536/23.6

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Primary Examiner: McElwain; Elizabeth F.

Parent Case Text

This application claims priority benefit of U.S. Provisional Application No. 60/149,050 filed Aug. 16, 1999, now abandoned.

Claims

What is claimed is:

1. A chimeric gene comprising an isolated ***nucleic acid*** fragment encoding a plant fatty acid modifying enzyme associated with conjugated double bond formation comprising a delta-9 position of fatty acids having an amino acid ***identity*** of at least 72.5% based on the Clustal method of alignment when compared to a polypeptide of SEQ ID NO:2 or 4

wherein said fragment or a functionally equivalent subfragment thereof or a complement thereof is operably linked to suitable regulatory sequences.

2. The chimeric gene of claim 1 wherein the ***nucleic acid*** fragment is isolated from Calendula officinalis.

3. The chimeric gene of claim 1 wherein the plant fatty acid modifying enzyme is associated with the formation of calendic acid.

4. A transformed host cell or plant comprising in its genome the chimeric gene of claim 1.

5. A transformed host cell or plant comprising in its genome the chimeric gene of claim 2.

6. A transformed host cell or plant comprising in its genome the chimeric gene of claim 3.

7. A method of altering the level of fatty acids in a host cell or plant wherein said fatty acids comprise a modification at a delta-9 position, said method comprising:

(a) transforming a host cell or plant with the chimeric gene of claim 1;

(b) growing the transformed host cell or plant under conditions suitable for the expression of the chimeric gene; and

(c) selecting those transformed host cells or plants having altered levels of fatty acids comprising a modified delta-9 position.

8. A method of altering the level of fatty acids in a host cell or plant wherein said fatty acids comprise a modification at a delta-9 position, said method comprising:

(a) transforming a host cell or plant with the chimeric gene of claim 2;

(b) growing the transformed host cell or plant under conditions suitable for the expression of the chimeric gene; and

(c) selecting those transformed host cells or plants having altered levels of fatty acids comprising a modified delta-9 position.

9. A method of altering the level of fatty acids in a host cell or plant wherein said fatty acids comprise a modification at a delta-9 position, said method comprising:

(a) transforming a host cell or plant with the chimeric gene of claim 3;

(b) growing the transformed host cell or plant under conditions suitable for the expression

of the chimeric gene; and

(c) selecting those transformed host cells or plants having altered levels of fatty acids comprising a modified delta-9 position.

10. The method of claim 7, 8, or 9 wherein the host cell or plant is selected from the group consisting of plant cells and microorganisms.

11. The method of claim 7, 8, or 9 and wherein the level of calendic acid is altered.

12. A method for producing fatty acid modifying enzymes associated with modification of a delta-9 position of fatty acids which comprises:

(a) transforming a microbial host cell with the chimeric gene of claim 1;

(b) growing the transformed host cell under conditions suitable for the expression of the chimeric gene; and

(c) selecting those transformed host cells containing altered levels of protein encoded by the chimeric gene.

13. A method for producing fatty acid modifying enzymes associated with modification of a delta-9 position of fatty acids which comprises:

(a) transforming a microbial host cell with the chimeric gene of claim 2;

(b) growing the transformed host cell under conditions suitable for the expression of the chimeric gene; and

(c) selecting those transformed host cells containing altered levels of protein encoded by the chimeric gene.

14. A method for producing fatty acid modifying enzymes associated with modification of a delta-9 position of fatty acids which comprises:

(a) transforming a microbial host cell with the chimeric gene of claim 3;

(b) growing the transformed host cell under conditions suitable for the expression of the chimeric gene; and

(c) selecting those transformed host cells containing altered levels of protein encoded by the chimeric gene.

15. The method of claim 12, 13, or 14 wherein the fatty acid modifying enzyme is associated with the formation of calendic acid or dimorphecolic acid.

United States Patent **6,590,141**
Frohberg **July 8, 2003**

Nucleic acid molecules from plants encoding enzymes which participate in starch synthesis

Abstract

Nucleic acid molecules are described which encode enzymes which participate in starch synthesis in plants. These enzymes are a new isoform of starch synthase. There are furthermore described vectors for generating transgenic plant cells and plants which synthesize a modified starch. There are furthermore described methods for the generation of these transgenic plant cells and plants, and methods for producing modified starches.

Inventors: **Frohberg; Claus** (Berlin, DE)
Assignee: **Aventis CropScience GmbH** (Frankfurt, DE)
Appl. No.: **638524**
Filed: **August 11, 2000**

Foreign Application Priority Data

Aug 11, 1999[DE] 199 37 348

Current U.S. Class: **800/284**; 800/278; 800/286; 800/320.1; 435/69.1; 435/101; 435/320.1; 435/419; 435/468; 536/23.6

Intern'l Class: C12N 015/29; C12N 015/82; C12N 005/04; A01H 005/00; C12P 019/04

Field of Search: 536/23.6 435/69.1,468,320.1,419,101 800/278,284,320.1,286

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Primary Examiner: Fox; David T.
Attorney, Agent or Firm: Frommer Lawrence & Haug LLP

Claims

I claim:

1. An isolated ***nucleic acid*** molecule encoding a protein with the bioactivity of a starch synthase selected from the group consisting of

(a) ***nucleic acid*** molecules which encode a protein with the amino acid sequence indicated under SEQ ID No. 2;

(b) ***nucleic acid*** molecules which encompass the nucleotide sequence shown under SEQ ID No. 1 or a complementary sequence thereof;

(c) ***nucleic acid*** molecules which encompass the coding region of the nucleotide sequence of the cDNA present in plasmid IR 65/87 (deposit number DSM 12970) or a complementary sequence thereof;

(d) ***nucleic acid*** molecules whose nucleotide sequence deviates from the sequence of the ***nucleic acid*** molecules mentioned under (a), (b) or (c) owing to the degeneracy of the genetic code;

(e) ***nucleic acid*** molecules which have over 85% sequence ***identity*** with SEQ ID NO:1; and

(f) ***nucleic acid*** molecules which constitute allelic variants of the nucleic acid molecules indicated under (a), (b), (c), (d) or (e).

2. The ***nucleic acid*** molecule as claimed in claim 1 which is a DNA molecule.

3. The ***nucleic acid*** molecule as claimed in claim 1 which is an RNA molecule.

4. A vector comprising a ***nucleic acid*** molecule as claimed in claim 1.

5. The vector as claimed in claim 4 comprising one or more regulatory elements which ensure the transcription of said ***nucleic acid*** molecules and/or the synthesis of a translatable RNA in a pro- and/or eukaryotic cell.

6. The vector as claimed in claim 4, wherein said ***nucleic acid*** molecule is linked in sense orientation to regulatory elements which ensure the transcription and synthesis of a translatable RNA in pro- and/or eukaryotic cells, or wherein said ***nucleic acid*** molecule is linked in anti-sense orientation to regulatory elements which ensure the transcription and synthesis of a non-translatable RNA in pro- and/or eukaryotic cells.

7. A host cell which is transformed with a ***nucleic acid*** molecule as claimed in claim 1 or a vector as claimed in claim 4, or a cell which is derived from the host cell and which comprises the vector of claim 4.

8. The host cell as claimed in claim 7 which is a plant cell.

9. A method for producing a protein encoded by the ***nucleic acid*** molecule of claim 1, in which a host cell as claimed in claim 7 is cultured under conditions which permit the synthesis of the protein, and the protein is isolated from the cultured cells and/or the culture medium.

10. The plant cell of claim 8, wherein said ***nucleic acid*** molecule which encodes a protein with the bioactivity of a starch synthase is under the control of regulatory elements which permit the transcription of a translatable mRNA in plant cells.

11. The plant cell of claim 8, wherein the activity of a protein encoded by the ***nucleic acid*** molecule of claim 1 is increased in this plant cell compared with corresponding, non-genetically-modified plant cells from wild-type plants.

12. A plant comprising plant cells as claimed in claim 8.

13. The plant as claimed in claim 12 which is a crop plant.

14. The plant as claimed in claim 12 which is a starch-storing plant.

15. The plant as claimed in claim 12 which is a maize plant.

16. A method for generating a transgenic plant cell, wherein a plant cell is subjected to genetic modification by introducing a ***nucleic acid*** molecule as claimed in claim 1 and/or a vector as claimed in claim 4.

17. A method for generating a transgenic plant, wherein

(a) a plant cell is subjected to genetic modification by introducing a ***nucleic acid*** molecule as claimed in claim 1 and/or a vector as claimed in claim 4; and

(b) a plant is regenerated from this cell; and, if appropriate,

(c) more plants are generated from the plant of (b).

18. Propagation material of a plant comprising plant cells as claimed in claim 8.

19. A method for producing a modified starch obtained from the host cell of claim 8, from the plant of claim 12, or from the propagation material of 18, comprising the step of extracting the starch from a plant cell as claimed in claim 8, from a plant as claimed in claim 12 and/or from propagation material as claimed in claim 18.

United States Patent **6,586,215**
Yaver , et al. **July 1, 2003**

Polypeptides having peroxidase activity and nucleic acids encoding same

Abstract

The present invention relates to isolated polypeptides having peroxidase activity and isolated nucleic acid sequences encoding the polypeptides. The invention also relates to nucleic acid constructs, vectors, and host cells comprising the nucleic acid sequences as well as methods for producing and using the polypeptides.

Inventors: **Yaver; Debbie** (Davis, CA); **McArdle; Barbara** (Davis, CA)
Assignee: **Novozymes Biotech, Inc.** (Davis, CA)
Appl. No.: **885329**
Filed: **June 19, 2001**

Current U.S. Class:	**435/192**; 435/6; 435/320.1; 435/325; 435/252.3; 536/23.1; 536/23.2
Intern'l Class:	C12N 009/08; C12N 015/00; C12N 005/00; C12Q 001/68; C07H 021/04
Field of Search:	435/192,6,252.3,320.1 536/23.2,23.1

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Primary Examiner: Monshipouri; M.
Attorney, Agent or Firm: Stames; Robert L.

Parent Case Text

CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation-in-part of U.S. application Ser. No. 09/596,824 filed Jun. 19, 2000 now U.S. Pat. No. 6,372,464 issued Apr. 16, 2002, which application is fully incorporated herein by reference.

Claims

What is claimed is:

1. An isolated ***nucleic acid*** sequence encoding a polypeptide having peroxidase activity, selected from the group consisting of:

(a) a ***nucleic acid*** sequence encoding a polypeptide having an amino acid sequence which has at least 75% ***identity*** with amino acids 22 to 370 of SEQ ID NO:2 or amino acids 19 to 362 of SEQ ID NO:6, or at least 85% ***identity*** with amino acids 22 to 385 of SEQ ID NO:4;

(b) a ***nucleic acid*** sequence encoding a polypeptide having an amino acid sequence which has at least 75% homology with nucleotides 772 to 2302 of SEQ ID NO:1 or nucleotides 2848 to 4247 of SEQ ID NO:5, or at least 85% homology with nucleotides 2008 to 3462 of SEQ ID NO:3;

(c) a ***nucleic acid*** sequence which hybridizes under high stringency conditions with (i) nucleotides 772 to 2302 of SEQ ID NO:1, nucleotides 2008 to 3462 of SEQ ID NO:3, or nucleotides 2848 to 4247 of SEQ ID NO:5, (ii) the cDNA sequence contained in nucleotides 772 to 2302 of SEQ ID NO:1, nucleotides 2008 to 3462 of SEQ ID NO:3, or nucleotides 2848 to 4247 of SEQ ID NO:5, or (iii) a complementary strand of (i) or (ii); and

(d) a fragment of (a), (b), or (c), which encodes a polypeptide having peroxidase activity.

2. The ***nucleic acid*** sequence of claim 1, which encodes a polypeptide having an amino acid sequence which has at least 75% ***identity*** with amino acids 22 to 370 of SEQ ID NO:2 or amino acids 19 to 362 of SEQ ID NO:6.

3. The ***nucleic acid*** sequence of claim 2, which encodes a polypeptide having an amino acid sequence which has at least 80% ***identity*** with amino acids 22 to 370 of SEQ ID NO:2 or amino acids 19 to 362 of SEQ ID NO:6.

4. The ***nucleic acid*** sequence of claim 3, which encodes a polypeptide of having an amino acid sequence which has at least 85% ***identity*** with amino acids 22 to 370 of SEQ ID NO:2 or amino acids 19 to 362 of SEQ ID NO:6.

5. The ***nucleic acid*** sequence of claim 4, which encodes a polypeptide having an amino acid sequence which has at least 90% ***identity*** with amino acids 22 to 370 of SEQ ID NO:2 or amino acids 19 to 362 of SEQ ID NO:6.

6. The ***nucleic acid*** sequence of claim 5, which encodes a polypeptide having an amino

acid sequence which has at least 95% ***identity*** with amino acids 22 to 370 of SEQ ID NO:2 or amino acids 19 to 362 of SEQ ID NO:6 .

7. The ***nucleic acid*** sequence of claim 1, which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6 .

8. The ***nucleic acid*** sequence of claim 1, which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6, or a fragment thereof having peroxidase activity.

9. The ***nucleic acid*** sequence of claim 1, which encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO6.

10. The ***nucleic acid*** sequence of claim 1, which encodes a polypeptide which consists of amino acids 22 to 370 of SEQ ID NO:2, amino acids 22 to 365 of SEQ ID NO:4, or amino acids 19 to 362 of SEQ ID NO:6.

11. The ***nucleic acid*** sequence of claim 1, which has at least 75% homology with nucleotides 772 to 2302 of SEQ ID NO:1 or nucleotides 2848 to 4247 of SEQ ID NO:5.

12. The ***nucleic acid*** sequence of claim 11, which has at least 80% homology with nucleotides 772 to 2302 of SEQ ID NO:1 or nucleotides 2848 to 4247 of SEQ ID NO:5.

13. The ***nucleic acid*** sequence of claim 12, which has at least 85% homology with nucleotides 772 to 2302 of SEQ ID NO:1 or nucleotides 2848 to 4247 of SEQ ID NO:5.

14. The ***nucleic acid*** sequence of claim 13, which has at least 90% homology with nucleotides 772 to 2302 of SEQ ID NO:1 or nucleotides 2848 to 4247 of SEQ ID NO:5.

15. The ***nucleic acid*** sequence of claim 14, which has at least 95% homology with nucleotides 772 to 2302 of SEQ ID NO:1 or nucleotides 2848 to 4247 of SEQ ID NO:5.

16. The ***nucleic acid*** sequence of claim 1, which has the ***nucleic acid*** sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:1.

17. The ***nucleic acid*** sequence of claim 1, which has the ***nucleic acid*** sequence of nucleotides 772 to 2302 of SEQ ID NO:1, nucleotides 2008 to 3462 of SEQ ID NO:3, or nucleotides 2848 to 4247 of SEQ ID NO:5.

18. The ***nucleic acid*** sequence of claim 1, which hybridizes under high stringency conditions with (i) nucleotides 772 to 2302 of SEQ ID NO:1, nucleotides 2008 to 3462 of SEQ ID NO:3, or nucleotides 2848 to 4247 of SEQ ID NO:5, (ii) me cDNA sequence contained in nucleotides 772 to 2302 of SEQ ID NO;1, nucleotides 2008 to 3462 of SEQ ID NO:3, or nucleotides 2845 to 4247 of SEQ ID NO:5, or (iii) a complementary strand of (i) or (ii).

19. The ***nucleic acid*** sequence of claim 1, which is contained in plasmid pBM37-7 which is contained in E. coli NRRL B-30280, plasmid pBM38-1 which is contained in E. coli NRRL B-30281, or plasmid pBM39-1 which is contained in E. coli NRRL B-30282.

20. A ***nucleic acid*** construct comprising the ***nucleic acid*** sequence of claim 1, operably linked to one or more control sequences which direct the production of the polypeptide in a suitable expression host.

21. A recombinant expression vector comprising the ***nucleic acid*** construct of claim 20, a promoter, and transcriptional and translational stop signals.

22. A recombinant host cell comprising the ***nucleic acid*** construct of claim 20.

23. A method for producing a polypeptide having peroxidase activity comprising

(a) cultivating the host cell of claim 22, under conditions suitable for production of the polypeptide; and

(b) recovering the polypeptide.

United States Patent **6,586,179**
Jegla , et al. **July 1, 2003**

Human Eag2

Abstract

The invention provides isolated nucleic acid and amino acid sequences of Eag2, antibodies to Eag2, methods of detecting Eag2, and methods of screening for modulators of Eag2 potassium channels using biologically active Eag2. The invention further provides, in a computer system, a method of screening for mutations of human Eag2 genes as well as a method for identifying a three-dimensional structure of Eag2 polypeptide monomers.

Inventors: **Jegla; Timothy J.** (Durham, NC); **Liu; Yi** (Cary, NC)
Assignee: **ICAgen, Incorporated** (Durham, NC)
Appl. No.: **614480**
Filed: **July 10, 2000**

Current U.S. Class:	**435/6**; 536/23.1; 435/69.1; 435/325; 435/320.1; 435/252.3; 530/350
Intern'l Class:	C12Q 001/68; C07H 017/00; C12P 021/06; C07K 014/00
Field of Search:	536/23.1 435/7.1,325,320.1,252.3 530/350 436/6

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Saganich et al., "Cloning of Components of a Novel Subthreshold-Activating K.sup.+ Channel With a Unique Pattern of Expression in the Cerebral Cortex," J. Neuroscience, vol. 19, No. 24, pp. 10789-10802 (1999).

Primary Examiner: Carlson; Karen Cochrane
Attorney, Agent or Firm: Townsend and Townsend and Crew LLP

Parent Case Text

CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority to U.S. Ser. No. 60/143,467, filed Jul. 13, 1999, herein incorporated by reference in its entirety.

Claims

What is claimed is:

1. An isolated ***nucleic acid*** encoding a polypeptide comprising an alpha subunit of a potassium channel, wherein the subunit:

(i) forms, with at least one additional Eag family alpha subunit, a potassium channel having the characteristic of voltage sensitivity; and wherein said ***nucleic acid*** specifically hybridizes under stringent conditions to SEQ ID NO:1, wherein the hybridization reaction is incubated at 42.degree. C. in a solution comprising 50% formamide, 5.times.SSC, and 1% SDS or at 65.degree. C. in a solution comprising 5.times.SSC and 1% SDS, with a wash in 0.2.times.SSC and 0.1% SDS at 65.degree. C.

2. An isolated ***nucleic acid*** encoding a polypeptide comprising an alpha subunit of a potassium channel, wherein the subunit:

(i) forms, with at least one additional Eag family alpha subunit, a potassium channel having the characteristic of voltage sensitivity; and

(ii) comprises an amino acid sequence that has greater than 85% amino acid ***identity*** to the amino acid sequence of SEQ ID NO:2.

3. The isolated ***nucleic acid*** of claim 1, wherein the polypeptide specifically binds to polyclonal antibodies generated against SEQ ID NO:2.

4. The isolated ***nucleic acid*** of claim 1, wherein the ***nucleic acid*** encodes human Eag2.

5. The isolated acid of claim 1, wherein the ***nucleic acid*** encodes an amino acid sequence of SEQ ID NO:2.

6. The isolated ***nucleic acid*** sequence of claim 1, wherein the ***nucleic acid*** has a nucleotide sequence of SEQ ID NO:1.

7. The isolated ***nucleic acid*** of claim 1, wherein the ***nucleic acid*** is amplified by primers that selectively hybridize under stringent hybridization conditions to the same sequence as primers selected from the group consisting of:

ATGCCGGGGGGCAAGAGAGGGCTG (SEQ ID NO:3);

CTGACCCTAAGCTCATAAGGATGAAC (SEQ ID NO:4);

CCACCTCATCATCCTGGATGACTTCC (SEQ ID NO:5);

TTAAAAGTGGATTTCATCTTTGTCAGATTCAGG (SEQ ID NO :6);

GGGGACCTCATTTACCATGCTGGAG (SEQ ID NO:7);

GATTCCCTCATCCACATTTTCAAAGGC (SEQ ID NO:8);

and wherein the hybridization reaction is incubated at 42.degree. C. in a solution comprising 50% formamide, 5.times.SSC, and 1% SDS or at 65.degree. C. in a solution comprising 5.times.SSC and 1% SDS, with a wash in 0.2.times.SSC and 0.1% SDS at 65.degree. C.

8. The isolated ***nucleic acid*** of claim 1, wherein the polypeptide monomer comprises an alpha subunit of a homomeric channel.

9. The isolated ***nucleic acid*** of claim 1, wherein the polypeptide monomer comprises an alpha subunit of a heteromeric channel.

10. An expression vector comprising the ***nucleic acid*** of claim 1.

11. A host cell transfected with the vector of claim 10.

12. A method of detecting a ***nucleic acid,*** the method comprising contacting a sample comprising a first ***nucleic acid*** with an isolated second nucleic acid of claim 1 and

detecting hybridization of the second ***nucleic acid*** to the first ***nucleic acid,*** thereby detecting the first ***nucleic acid***.

United States Patent **6,583,337**
Allen , et al. **June 24, 2003**

Plant glucose-6-phosphate translocator

Abstract

This invention relates to an isolated nucleic acid fragment encoding a glucose-6-phosphate/phosphate translocator. The invention also relates to the construction of a chimeric gene encoding all or a portion of the glucose-6-phosphate/phosphate translocator, in sense or antisense orientation, wherein expression of the chimeric gene results in production of altered levels of the glucose-6-phosphate/phosphate translocator in a transformed host cell.

Inventors: **Allen; Stephen M.** (Wilmington, DE); **Rafalski; J. Antoni** (Wilmington, DE)

Assignee: **E. I. du Pont de Nemours and Company** (Wilmington, DE)

Appl. No.: **436521**

Filed: **November 9, 1999**

Current U.S. Class: **800/278**; 435/6; 435/69.1; 435/71.1; 435/183; 435/410; 435/419; 435/418; 435/252.3; 435/320.1; 530/350; 530/370; 536/23.1; 536/23.2; 536/23.6; 536/24.1; 536/24.3; 536/24.5

Intern'l Class: A01H 003/00; C07H 021/04; C07K 014/415; C12N 005/14; C12N 009/00

Field of Search: 435/6,69.1,71.1,183,410,419,418,252.3,320.1 530/370,350 536/23.1,23.2,23.6,24.1,24.3,24.5

References Cited [Referenced By]

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Foreign Patent Documents

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Bork. Genome Research vol. 10, p. 398-400, 2000.*
Kammerer, B. et al. (1998) The Plant Cell 10:105-117.
Denyer et al. (1996) Plant Physiol. 112:779-785.
Thorbjornsen et al. (1996) Plant J. 10:243-250.
NCBI General Identifier No. 2997591.
NCBI General Identifier No. 2997589.

Primary Examiner: Bui; Phuong T.

Parent Case Text

This application claims priority benefit to U.S. Provisional Application No. 60/107,910 filed Nov. 10, 1998, now abandoned.

Claims

What is claimed is:

1. An isolated ***polynucleotide*** comprising:

(a) a nucleotide sequence encoding a polypeptide having glucose-6-phosphate/phosphate translocator activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:4 have at least 86% sequence ***identity*** based on the Clustal alignment method, or

(b) the complement of the nucleotide sequence, wherein the complement and the nucleotide sequence contain the same number of nucleotides and are 100% complementary.

2. The ***polynucleotide*** of claim 1, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:4 have at least 90% sequence ***identity*** based on the Clustal alignment method.

3. The ***polynucleotide*** of claim 1, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:4 have at least 95% sequence ***identity*** based on the Clustal alignment method.

4. The ***polynucleotide*** of claim 1, wherein the nucleotide sequence comprises the nucleotide sequence of SEQ ID NO:3.

5. The ***polynucleotide*** of claim 1, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:4.

6. A recombinant DNA construct comprising the ***polynucleotide*** of claim 1 operably linked to a regulatory sequence.

7. A method for transforming a cell comprising transforming a cell with the ***polynucleotide*** of claim 1.

8. A cell comprising the recombinant DNA construct of claim 6.

9. A method for producing a plant comprising transforming a plant cell with the ***polynucleotide*** of claim 1 and regenerating a plant from the transformed plant cell.

10. A plant comprising the recombinant DNA construct of claim 1.

11. A seed comprising the recombinant DNA construct of claim 1.

12. A vector comprising the ***polynucleotide*** of claim 1.

United States Patent **6,582,950**
Smith , et al. **June 24, 2003**

C3 binding polypeptide of Streptococcus agalactiae group b Streptococcus

Abstract

This invention relates to the identification of a human complement C3 binding polypeptide and the nucleic acid which encodes the polypeptide from Streptococcus agalactiae. The polypeptide binds C3 and may be implicated in S. agalactiae adhesion and/or virulence. The polypeptide is conserved in mass in a variety of streptococcal isolates and is recognized by antibodies produced by humans exposed to or colonized with Group B Streptococcus.

Inventors: **Smith; Beverly L.** (Minneapolis, MN); **Ferrieri; Patricia** (Minneapolis, MN)

Assignee: **Regents of the University of Minnesota** (Minneapolis, MN)

Appl. No.: **610199**

Filed: **July 1, 2000**

Current U.S. Class: **435/252.3**; 435/320.1; 435/325; 536/23.7

Intern'l Class: C12N 001/20; C12N 015/00; C12N 005/00; C07H 021/04

Field of Search: 424/190.1 435/69.3,252.33,253.4,252.3,320.1,325 536/23.7

References Cited [Referenced By]

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Foreign Patent Documents

WO 98/21337	May., 1998	WO.

Other References

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Wilkinson, "Comparison of Streptococcal R Antigens," Applied Microbiology, 24(4):669-670 (1972).

Primary Examiner: Navarro; Mark
Attorney, Agent or Firm: Mueting Raasch & Gebhardt

Parent Case Text

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit under 35 U.S.C. .sctn.119(e) of U.S. Provisional Patent Application No. 60/157,550, filed on Oct. 4, 1999, and U.S. Provisional Patent Application No. 60/173,766, filed on Dec. 30, 1999, both of which are hereby incorporated by reference.

Claims

What is claimed is:

1. An isolated ***nucleic acid*** fragment that hybridizes to at least a portion of at least one of the ***nucleic acid*** fragments represented by SEQ ID NO:6 or SEQ ID NO:4 or their

complementary strands under hybridization conditions of prehybridization for 1 hour at 62.degree. C. in hybridization solution (5.times.SSC (1.times.SSC is 0.15 M NaCL, 0.015 M sodium citrate), 0.02% sodium dodecyl sulfate (SDS), 0.1% N-lauroylsarcosine, 1% Blocking Reagent) followed by two stringency washes with 2.times.SSC, 0.1% SDS for 5 minutes at room temperature and once with 0.5.times.SSC, 0.1% SDS for 15 minutes at 62.degree. C., said isolated ***nucleic acid*** fragment encodes a polypeptide that binds human complement C3 protein.

2. The ***nucleic acid*** fragment of claim 1 isolated from S. agalactiae.

3. The ***nucleic acid*** fragment of claim 1 which encodes a polypeptide represented by. SEQ ID NO:5.

4. The ***nucleic acid*** fragment of claim 1 in a ***nucleic acid*** vector.

5. The ***nucleic acid*** fragment of claim 4 wherein the ***nucleic acid*** vector is an expression vector capable of producing a polypeptide.

6. An isolated ***nucleic acid*** having at least 50% ***nucleic acid identity*** to the ***nucleic acid*** fragments represented by SEQ ID NO:6 or SEQ ID NO:4, and which hybridizes under hybridization conditions of prehybridization for 1 hour at 62.degree. C. in hybridization solution (5.times.SSC (1.times.SSC is 0.15 M NaCL, 0.015 M sodium citrate), 0.02% sodium dodecyl sulfate (SDS), 0. 1% N-lauroylsarcosine, 1% Blocking Reagent) followed by two stringency washes with 2.times.SSC, 0.1% SDS for 5 minutes at room temperature and once with 0.5.times.SSC, 0.1% SDS for 15 minutes at 62.degree. C., to at least a portion of at least one of the ***nucleic acid*** fragments represented by SEQ ID NO:6 or SEQ ID NO:4 or their complementary strands, said ***nucleic acid*** encoding a polypeptide that binds human complement C3 protein.

7. An isolated ***polynucleotide*** encoding a polypeptide comprising the amino acids represented by SEQ ID NO:5.

8. The ***polynucleotide*** of claim 7 wherein the polypeptide binds human complement C3.

9. An isolated host cell comprising a ***nucleic acid*** fragment of claim 1.

10. The cell of claim 9 wherein the cell is a bacterium or a eukaryotic cell.

11. An isolated ***nucleic acid*** fragment comprising SEQ ID NO:6 or SEQ ID NO:4 or their complementary strands.

12. An isolated RNA transcribed from a double-stranded ***nucleic acid*** comprising a ***nucleic acid*** fragment of claim 2.

13. An isolated ***nucleic acid*** fragment encoding a polypeptide having at least 50% amino acid ***identity*** to SEQ ID NO:5, said polypeptide binds to human complement C3 protein.

14. An isolated ***nucleic acid*** fragment encoding a polypeptide having at least 60% amino acid ***identity*** to SEQ ID NO:5, said polypeptide binds to human complement C3 protein.

15. An isolated ***nucleic acid*** fragment encoding a polypeptide having at least 70% amino acid ***identity*** to SEQ ID NO:5, said polypeptide binds to human complement C3 protein.

16. An isolated ***nucleic acid*** fragment encoding a polypeptide having at least 80% amino acid ***identity*** to SEQ ID NO:5, said polypeptide binds to human complement C3 protein.

17. An isolated ***nucleic acid*** fragment consisting essentially of at least 30 nucleotides of SEQ ID NO:4, wherein said ***nucleic acid*** fragment encodes a polypeptide that binds to human complement C3 protein.

United States Patent **6,541,684**
Bowen , et al. **April 1, 2003**

Nucleotide sequences encoding maize RAD51

Abstract

Nucleic acid sequences encoding two RAD51 recombinases active in maize plants are provided. cDNA sequences including the ZmRAD51 coding sequences and unique 3'-untranslated regions which are useful as RFLP probes, are also provided. The production of plasmids containing a nucleic acid sequence encoding a ZmRAD51 fusion protein, as well as the use of the plasmids to introduce the ZmRAD51 coding sequence into a host cell, such as maize cell, are also disclosed.

Inventors: **Bowen; Benjamin A.** (Hayward, CA); **Chamberlin; Mark A.** (Windsor Heights, IA); **Drummond; Bruce J.** (Des Moines, IA); **McElver; John A.** (Durham, NC); **Rothstein; Rodney J.** (Maplewood, NJ)

Assignee: **Trustees of Columbia University in the City of New York** (New York, NY); **Pioneer Hi-Bred International, Inc.** (Johnston, IA)

Appl. No.: **246963**

Filed: **February 9, 1999**

Current U.S. Class: **800/320.1**; 435/69.1; 435/196; 536/23.1; 536/23.5; 536/24.1

Intern'l Class: A01H 005/00

Field of Search: 536/23.1,23.5,24.1 435/410,468,196,69.1 800/298,320.1

References Cited [Referenced By]

Foreign Patent Documents

WO 93/22443	Nov., 1993	WO.
WO 97/41228	Nov., 1997	WO.

Other References

Natalie Teager et al, Isolation and characterization of rad51 orthologs from Coprinus cinereus and Lycopersicon esculentum, and phylogenetic analysis of eukaryotic recA homologs, Curr Genet 1997, 31: 144-157.*
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Sung, 1994. Catalysis of ATP-Dependent Homologous DNA Pairing and Strand Exchange by Yeast RAD51 Protein. Science, vol. 265, 1241-1243.
Stassen, et al. Isolation and characterization of rad51 orthologs from Coprinus cinereus and Lycopersicon esculentum, and phylogenetic analysis of eukaryotic recA homologs. Curr Genet (1997) 31: 144-157.
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Benson, et al. 1998. Synergistic actions of Rad51 and Rad52 in recombination and DNA repair. Nature, vol. 391, 401-404.
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Smith, K.N., et al. 1996. Untitled. Embl. Sequence Data Library, XP002105502, Accession No. U43528.

Primary Examiner: Ketter; James
Attorney, Agent or Firm: Foley & Lardner

Parent Case Text

CROSS REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application No. 60/074,745, filed Feb. 13, 1998 and is herein incorporated by reference.

Claims

What is claimed is:

1. An isolated polynucleotide comprising a member selected from the group consisting of:

a) a polynucleotide encoding a polypeptide selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 7;

b) a polynucleotide having at least 90% identity to a polynucleotide of (a);

c) a polynucleotide which will hybridize under ***stringent hybridization*** conditions to said polynucleotide of (a) or (b); and

d) a polynucleotide comprising at least 30 contiguous nucleotides from a polynucleotide of (a), (b) or (c);

wherein the polynucleotide of (a), (b) or (c) encodes a polypeptide with recombinase activity.

2. The isolated polynucleotide of claim 1, wherein said polynucleotide has a sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 6.

3. An expression cassette comprising a polynucleotide of claim 1 operably linked to a promoter.

4. The host cell transfected with an expression cassette of claim 3.

5. The host cell of claim 4, wherein said host cell is a bacterial cell.

6. The host cell of claim 4, wherein said host cell is a sorghum or maize cell.

7. A method of making maize recombinase comprising the steps of:

a) transforming or transfecting a host cell with the expression cassette of claim 3; and

b) purifying the recombinase from the host cell.

8. The method of claim 7, wherein the host cell is selected from the group consisting of a bacterial cell, a plant cell, a mammalian cell and a yeast cell.

9. A method of modulating ZmRAD 51 activity in a plant, comprising:

(a) introducing into a plant cell an expression cassette comprising an isolated polynucleotide of claim 1 operatively linked to a promoter;

(b) culturing the plant cell under plant cell growing conditions;

(c) regenerating a plant which possesses the transformed genotype, and

(d) inducing expression of said polynucleotide for a time sufficient to modulate ZmRAD51 activity in said plant.

10. A transgenic plant cell comprising an isolated polynucleotide of claim 1.

11. A transgenic plant comprising an isolated polynucleotide of claim 1.

12. A transgenic seed from the transgenic plant of claim 11.

13. Primer pairs for isolating at least a part of a Zea mays recombinase gene, selected from the group consisting of SEQ ID NOS: 12 and 13, SEQ ID NOS: 14 and 19, SEQ IDS NOS: 14 and 20, and SEQ ID NOS: 14 and 15, or complements thereof.

14. An RFLP probe for a maize recombinase gene comprising at least 30 nucleotides residues of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, or SEQ ID NO: 11.

Attorney's Docket No.: 09010-003005

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Mathur, et al.
Serial No. : 09/880,729
Filed : June 12, 2001
Title : ENZYMES HAVING CARBOXYMETHYL CELLULASE ACTIVITY AND METHODS OF USE THEREOF

Art Unit : 1652
Examiner : Manjunath N. Rao, Ph.D.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

1. I, Jay M. Short, am a co-inventor with David E. Lam and Eric J. Mathur, on the above-identified patent application.

2. I am an expert in the field of molecular biology and enzyme development and was an expert at the time of the invention. I am presently employed as CEO and as a research scientist at Diversa Corporation, San Diego, CA, assignee of the above-referenced patent application. My resume is attached as documentation of my credentials.

3. I declare that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for carboxymethyl cellulase activity, was very high. Using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of nucleic acids encoding the exemplary carboxymethyl cellulase of the invention and screen them for expression of polypeptides having carboxymethyl cellulase activity. One skilled in the art could have used routine protocols known

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

9/23/03
Date of Deposit

Jeanne Anour Rice
Signature

Jeanne Anour Rice
Typed or Printed Name of Person Signing Certificate

in the art at the time of the invention, including those described in the instant specification, to screen for nucleic acids encoding polypeptides having at least 50% percent sequence identity to SEQ ID NO:1, or active fragments thereof, for carboxymethyl cellulase activity. While the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (i.e., finding variant nucleic acids encoding carboxymethyl cellulases) predictable. Furthermore, it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with carboxymethyl cellulase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides having carboxymethyl cellulase activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including making and using a genus of nucleic acids encoding carboxymethyl cellulases.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted

Date:_____

_____

Jay M. Short

CURRICULUM VITAE

NAME: Jay M. Short, Ph.D.

EDUCATION:

1981 - 1985	Ph.D., Biochemistry Case Western Reserve University, Cleveland, Ohio
1980 - 1981	Graduate Study, Macromolecular Science Case Western Reserve University, Cleveland, Ohio
1976 - 1980	B.A. with Honors, Chemistry Taylor University, Upland, Indiana

RESEARCH & PROFESSIONAL EXPERIENCE:

1999 - present	**CEO, President, Chief Technology Officer & Board of Directors** Diversa Corporation San Diego, California
1998 - present	**President, Chief Technology Officer & Board of Directors** Diversa Corporation San Diego, California
1997 - 1998	**Executive Vice President, Chief Technology Officer & Board of Directors** Diversa Corporation San Diego, California
1994 - 1997	**Chief Technology Officer & Board of Directors** Diversa Corporation San Diego, California
1990 - 1994	**President** Stratacyte, Inc. La Jolla, California
1992 - 1994	**Vice President** R&D (Research) and Operations Stratagene Cloning Systems La Jolla, California
1989 - 1992	**Vice President** R&D (Research) and Biological Operations Stratagene Cloning Systems
1988 - 1989	**Senior Staff Scientist** Research and Development Stratagene Cloning Systems

1985 - 1988	**Staff Scientist** Research and Development Stratagene Cloning Systems
1981 - 1985	**Ph.D. Research** Case Western Reserve University Dr. Richard W. Hanson's Laboratory, Identification and characterization of the promoter for P-enolpyruvate carboxykinase. First identification of a cAMP regulatory domain.
1980 - 1981	**Graduate Student Research** Case Western Reserve University Dr. Bruce Roe's Laboratory, Analysis of the cellulase activity of *Trichoderma viride*.

TEACHING EXPERIENCE:

Thesis Advisor (1988-1993), University of Uppsala, Sweden, Ph.D. for Michelle Alting-Mees
Lecturer (1992), Committee for Advanced Scientific Education, Center for Drug Evaluation and Research, FDA.
Faculty (1989), Transgenic Mouse Model and Its Application in Assessing *In Vivo* Mutagenesis, Genetic Toxicology Workshop (3rd Annual). Microbiological Associates Inc. Bethesda, MD.
Faculty (1987), DNA Cloning and Expression. Physiology Society Workshop. San Diego, CA.
Teaching Assist., (1981-1985). Molecular and Cellular Biology. Case Western Reserve University.
Teaching Assist., (1981). Physiological Chemistry. Kent State Univ., Kent, OH.
Teaching Assist., (1978-1980). Quantitative Analysis. Taylor University.

AWARDS, PROFESSIONAL MEMBERSHIPS, ACCOMPLISHMENTS, AND ACTIVITIES:

Visiting Scientist, International Centre of Insect Physiology and Ecology (ICIPE), Kenya (2002-2004)
Science & Technology Committee, *BIOCOM San Diego*
Advisory Board, IngleWood Ventures
Finalists for UCSD Connect's Most Innovative New Product Award in the Biotechnology R&D Category
Advisory Board, *Chemical & Engineering News*
Board of Advisors and Founding Member, Division of Biological Sciences, *UCSD*
Board Director, *BIOCOM San Diego*
Chairman of the Board, Innovase
Board Director, Zymetrics
Board Director, Innovase
Director at Large, *YPO (Young Presidents' Organization) San Diego.*
2001 T-Sector Life Science Innovator Award.
2001 Deloitte and Touche's Orange County / San Diego 2001 Technology "Fast 50".
San Diego Entrepreneur of the Year 2001.
YPO (Young Presidents' Organization) San Diego.
YPO (Young Presidents' Organization) International.
Finalist for San Diego Entrepreneur of the Year in 2000.
Largest Biotechnology IPO raising over $200MM.
Founding management member of Diversa Corporation.
Panel for Chemical Science & Technology for NIST, appointed by the National Research Council (1997-2000).
Chairman (1993), Discussion Group, Society of Toxicology Conference.
U.S. Committee Member for Evaluation of Biotechnology Research in Spain.
Editor, Mutation Research.

UCSD Connect Program (1991) 1st Place Award for Innovation and Entrepreneurship in Biotechnology (over 50 competing biotech companies).
UCSD Connect Program (1990) 1st Place Award for Innovation and Entrepreneurship in Biotechnology.
Consultant for European Economic Community on Transgenic Toxicology Testing (91-94).
The New York Academy of Sciences.
Reviewer for *Proceedings of the National Academy of Sciences*, *Genetic Analysis Techniques, Analytical Biochemistry, & Nucleic Acids Research.*
American Association for the Advancement of Science.
American Chemical Society.
American Society of Biochemistry and Molecular Biology.
American Society of Microbiology.
Environmental Mutagenesis Society.
Society for Industrial Microbiology
Society of Toxicology.
Japanese Environmental Mutagen Society.
Who's Who Registry of Business Leaders (1994-1995)
American Men and Women of Science (1995)
NIEHS Peer Review Committee.
SBIR Study Section.
SBIR Annual Report (1993) Program Success Profile (Top 8 of 800 Companies).
Stratagene (1990) Innovation Award - Lambda ZAP® vector.
Stratagene (1990) Service Award
Stratagene (1991) Innovation Award - Big Blue® Transgenic Testing System.
Stratagene (1992) Most Innovative Award - Managers/Supervisors.
Institutional Animal Care and Use Committee (IACUC), Chairman and Institutional Official.
Award from the University of Victoria for Contributions to the Development of Short-term Transgenic Mutation Assays.
Nominated as Council Member for the U.S. Environmental Mutagen Society.
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Board Director & Secretary, *Stressgen Therapeutics, Victoria, BC, Canada*
Board Director, *Diversa, La Jolla, CA*
Board Director, *Invitrogen, Carlsbad, CA*
Consultant, *Stratagene Cloning Systems, La Jolla, CA*
Consultant, *Micro Product Systems, Lynn, IN*
Reviewer for U.S. Congressional Office of Technology Assessment (OTA) on *The Human Genome Project and Patenting DNA Sequences.*

MEDIA:

ABC Discovery News, ABC San Diego Channel 10, BBC Radio, Bioinformed Newsletter, Biotechnology Newsletter, BioVentures View, Business Daily, Business Week, CEO Cast, Chemical Engineering, Chemical Week, Chemistry & Industry (UK), CNBC, CNN Science & Technology, dBusiness.com, Discovery Magazine, Forbes.com, Good Morning America, Horizon Air Magazine, Idea TV, Inside Business Radio Show, JAG Financial News, Los Angeles Times, NBC San Diego Channel 7/39, National Radio Report, New York Times, Pirateinvestor.com, R&D Magazine, RTL German Television, Reuters, San Diego Business Transcript, San Diego Channel KUSI, San Diego Channel 10, San Diego Magazine, San Diego Union Tribune, Scientist, Time Magazine, The Discovery Channel, The Motley Fool, Time Magazine, USA Today, Wall Street Journal, Wall Street Transcript, Washington Post

PATENTS:

DNA Cloning Vectors with *in vivo* Excisable Plasmids (1987).
Mutagenesis Testing Using Transgenic Animals Carrying Marker Genes (1987).
Mutagenesis Testing Using Transgenic Non-Human Animals Carrying Test

DNA Sequences (1987).
Dietary and Hormonal Regulation of Expression of Exogenous Genes in Transgenic Animals Under Control of the Promoter of the Gene Phosphoenolpyruvate Carboxykinase (1988).
A Transgenic Mouse for Measurement and Characterization of Mutation Induction *In Vivo* (1989).
Rapid Screening Mutagenesis and Teratogenesis Assay (1989).
A Combinatorial Approach to Regenerating the Immunoglobulin Repertoire in Prokaryotic Cells (1990).
Transgenic Animal Models for *In Vivo* Mutagenesis Testing (1990).
Polycos Vectors (1991).
A Lambda Packaging Extract Lacking β-Galactosidase Activity (1991).
A System for Regulation of Eukaryotic Genes (1991).
Methods for Phenotype Creation from Multiple Gene Populations (1991).
Transgenic Non-Human Animals Carrying Test DNA Sequences (1992).
Mutagenesis Testing Using Transgenic Non-Human Animals Carrying Test DNA Sequences (1992).
Selectable System Patent (1992).
Polycos Mutagenesis Systems (1993).
Use of Trans-acting Proteins for the Development of an *In Situ* Expression Screening System (1993).
Enzyme Kits and Libraries (1995).
Enzyme Activity Screening of Clones having DNA from Uncultivated Microorganisms (1995).
Enzyme Tiered (1995).
Method for Screening for Enzyme Activity (1995).
Combined Enzyme Screening/Evolution (1995).
Uncultured/Activity Screening (1995).
Directed Evolution of Thermophilic Proteins (1995).
Combinatorial Enzyme Development (Directed Mutagenesis) (1996).
Protein Activity Screening of Clones having DNA from Uncultivated Microorganisms (1996).
Production and Use of Normalized DNA Libraries (1996).
Methods of DNA Shuffling with Polynucleotides Produced by Blocking or Interrupting a Synthesis or Amplification Process (1996).
Method of Screening for Enzyme Activity (Biopanning) (1996).
Directed Evolution of Thermophilic Enzymes (1996).
Environmental Biopanning (1996).
Combinatorial Enzyme Development (1996).
Enzyme Activity Screening of Clones Having DNA from Uncultivated Miroorganisms (1996).
Normalized Samples/Libraries (1996).
Reassembled Pools of Mutagenized DNA & Procedure (1996).
Fluorescent-based Single Screening for Enzymes (1996).
High Throughput Screening for Novel Enzymes (1997).
Nucleotide Sequence of the *Aquifex aeolicus* Genome, Fragments Thereof, and Uses Thereof (1997).
Screening for Novel Bioactivities (1997).
Screening for Novel Compounds which Regulate Biological Interactions (1997).
Method for Screening Enzyme Activity (1997).
High Throughput Screening for Novel Enzymes (1997).
"Discovery" (whole process, including uncultivated, normalized, biopanning, screening, evolving, (etc.) (1997).
Production of Enzymes Having Desired Activities By Mutagenesis (1999).
Protein Activity Screening of Clones Having DNA from Uncultivated Microorganisms (1999).
Method of DNA Reassembly by Interrupting Sythesis (1999).
Production and Use of Normalized DNA Libraries (1999).
Enzyme Kits and Libraries (1999).
Screening for Novel Bioactivities (2000).
Method for Screening for Enzyme Activity (2000).
Screening for Novel Bioactivities (2000).
Production and Use of Normalized DNA Libraries (2000).
Method of Screening for Enzyme Activity (2000).
Screening Methods for Enzymes and Enzyme Kits (2001).
Saturation Mutagenesis in Directed Evolution (2001).
High Throughput Screening for Novel Enzymes (2001).

Recombinant Bacterial Phytases and Uses Thereof (2001).
Methods Useful for Nucleic Acid Sequencing Using Modified Nucleotides Comprising Phenylboronic Acid (2001).
End Selection in Directed Evolution (2001)
Gene Expression Library Produced From DNA From Uncultivated Microorganisms and Method for Making the Same (2001)
Directed Evolution of Thermophilic Enzymes (2002)
Method for Screening for Enzyme Activity (2002)
Exonuclease-Mediated Gene Assembly in Directed Evolution (2002)
End Selection In Directed Evolution (2002)
Exonuclease-Mediated Gene Assembly in Directed Evolution (2002)
Screening for Novel Bioactivities(2002)
Method of DNA Shuffling with Polynucleotides Produced or Blocking or Interrupting Synthesis or Amplification Process (2002)
Production and Use of Normalized DNA Libraries (2002)
Sequence Based Screening (2002)
Non-Stochastic Generation of Genetic Vaccines (2002)
Over 100 Additional Pending Patent Applications Worldwide.

GRANTS AND CONTRACTS:

*Phase I Small Business Contract #N43-Am-62282. 1985 - 1986. P.I.
Vectors and Techniques for Rapid DNA Sequencing.
*Phase II Small Business Contract #N43-Am-62282. 1988 - 1990. P.I.
Vectors and Techniques for Rapid DNA Sequencing.
*Phase I Small Business Grant 2R43ES04484-02. 1986 - 1987. P.I.
Identification of Genetic Lesions Leading to Mutations.
*Phase II Small Business Grant 2R43ES04484-02. 1989 - 1992. P.I.
Identification of Genetic Lesions Leading to Mutations.
*1R01-ES04728-01A1. 1989 - 1992. (NIEHS) P.I.
Animal Model for Identification of Genetic Lesions.
*Phase I Small Business Grant #R43GM42291-01. 1989. P.I.
Switch Mechanism for Gene Expression in Transgenics.
*RFP NIH-ES-88-11. 1989-1994. (NIEHS) Co-I.
Development of Mutagenesis Assays Using Transgenic Mice.
*Phase II Small Business Grant #2R44GM42291-02. 1990-1992. (DRG/NIH) P.I.
Switch Mechanism for Gene Expression in Transgenics.
*Phase I Small Business Grant #1R43GM46585-01. 1991. (DRG/NIH) P.I.
Generation of a Peptide Screening System Through the Development of Combinatorial-splicing "Polycos" Vectors.
*Phase I Small Business Grant #1R43CA57066-01. 1992. (NCI) P.I.
Transgenic Rats: A Short-term Mutagenicity Assay for Multi-species Testing of Suspected Human Carcinogens.
*Phase I Small Business Grant #1R43GM48300-01. 1992. (DRG/NIH) P.I.
Analysis of the Immunoglobulin Hypermutator Mechanism.
*Phase I Small Business Grant #1R43ES06146-01. 1992. (NIEHS) P.I.
Selectable "Polycos" Shuttle Vectors for In Vivo Mutagenicity Testing.
*Phase II Small Business Grant #2R44GM46585-02. 1992-1994. (NIGMS) P.I.
Peptide Screening Utilizing Combinatorial Polycos Vector.
*Phase I Small Business Grant #1R43RR08667-01. 1992-1993. (DRG/NIH) Co-I.
A One-step PCR Cloning System Based on FLP Recombination.
*Phase II Small Business Grant #2R44CA57066-02. 1993-1995. (NCI) P.I.
Transgenic Rats:Transgenic Rat Model for Mutagenicity Testing.
*Phase I Small Business Grant. 1993-1994. (NIH) Co-I.
Transgenic Fish Model for Mutagenicity Testing.
*Phase II Small Business Grant (1994-1996). (NIH) P.I.
"Polycos" Shuttle Vectors for Mutagenicity testing.
*Phase I Small Business Grant. 1994. (NIH) Co-I.
Vector System for Studying Protein-Protein Interactions.

*CRADA with LLNL. 1994. (NIH) Co-I.
Mouse and Rat Painting Probes.
*CRADA with FDA. 1994. (NIH) Co-I.
Tamoxifen Testing in F-344 Rats.
*CRADA with NASA. 1994. (NIH) Co-I.
Radiation Damage in the Microgravity Environment.

ABSTRACTS AND INVITED LECTURES:

Over 200 Abstracts and Invited Lectures.

PUBLICATIONS:

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